



Case Report

Treatment of ovarian endodermal sinus tumor to preserve fertility

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Abstract

Endodermal sinus tumor, also known as yolk sac tumor (YST), is a malignant germ cell tumor that most frequently occurs in the testis, the ovary, and sacrococcygeal areas in children. YSTs are highly aggressive and because of the early metastatic or invasive pattern, their prognosis has been poor. Treatment methods for YSTs are usually intensive, including multiagent chemotherapy, and have shown to improve patient survival significantly; therefore, it is important to consider the reproductive function of these patients with long-term survival. Herein, we present the case of a 31-year-old female, who was diagnosed with unilateral ovarian YST at the age of 13. The patient was treated with fertility-sparing surgery and postoperative adjuvant chemotherapy. During the subsequent long-term follow-up, she was not only free of disease, but also had a successful, naturally conceived pregnancy at 31 years of age. We, therefore, conclude that YST is a curable disease, and that fertility-preservation surgery and subsequent immediate combination chemotherapy is the treatment of choice.

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Keywords: endodermal sinus tumor; fertility; ovary; yolk sac tumor

1. Introduction

Because of the aggressive nature and occurrence of malignant germ cell tumor, such as endodermal sinus tumor, also known as yolk sac tumor (YST),¹ on the ovary or the testis in childhood or in the young adolescent period, greater concern about future fertility is needed. The feasibility of fertility-sparing surgery has been discussed at length for decades.² The main treatment modes are excision or complete removal of the disease sites by cystectomy, oophorectomy, or unilateral salpingo-oophorectomy, followed by multiagent chemotherapy.³ However, there have been some cases that showed menstrual disturbance and infertility, suggesting that ovarian damage or failure was due to the long-term side effects of

curative chemotherapy.⁴ In addition, recurrence of the malignant disease has also been noted in some cases with a curative status at long-term follow-up. Therefore, many concerns about the appropriate treatment for patients with malignant germ cell tumor have been raised. Herein, we present the case of a female patient who was diagnosed with right ovarian YST, underwent fertility-sparing surgery and treated with complete adjuvant chemotherapy at 13 years of age, and who had a naturally conceived pregnancy at the age of 31.

2. Case report

A 31-year-old female was diagnosed with right ovarian YST, surgical–pathological stage IC, when she was 13 years old. The patient underwent right salpingo-oophorectomy, appendectomy, multiple omentum biopsies, and pelvic lymph node sampling initially, followed by four courses of postoperative adjuvant chemotherapy with cisplatin, vinblastine, and bleomycin (PVB; 5-day 25-mg cisplatin, 1-day 15-mg vinblastine, and 1-day 25-mg bleomycin), and then two courses of adjuvant

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chemotherapy with a PV (cisplatin and vinblastine) regimen. A second-look operation was performed to confirm complete surgical–pathological remission. After the second-look operation, two additional courses of adjuvant chemotherapy with a PV regimen were prescribed. The serum levels of alpha-fetoprotein decreased from the initial level of 8672 ng/mL (normal <20 ng/mL) to 2.09 ng/mL after completing eight courses of adjuvant chemotherapy.

After treatment she had a regular menstrual cycle, and was able to conceive naturally and give birth to a healthy baby at 39 weeks of gestation at the age of 31.

3. Discussion

YST (endodermal sinus tumor) is the second most common malignant germ cell tumor of the ovary.⁵ Before the introduction of effective chemotherapy, the prognosis for patients diagnosed with YSTs involving surgical treatment was poor. Patients with YSTs had a 3-year survival rate of 13%.⁶ After combination chemotherapy was introduced, the survival rate improved dramatically.⁷ However, the standard therapeutic strategy remains uncertain. Because YSTs are rare and mostly occur in young girls or adolescents, deciding between preservation of the reproductive function and achievement of long-term survival is sometimes difficult.

Fertility-sparing surgery for patients with YSTs was found to be as effective as radical surgery.⁸ In addition, malignant germ

cell tumors, including YST, removed by conservative operation and treated with platinum-based chemotherapy might have excellent survival outcomes.⁹ Comprehensive staging after removing localized malignant germ cell tumors of the ovary is crucial and leads to a better outcome,¹⁰ although more conservative procedures, such as cystectomy, might be more beneficial to maintaining the future reproductive function, based on the experience of managing ovarian borderline tumors.^{11,12}

However, because all germ cell tumors are highly sensitive to chemotherapy, we can perform fertility-preservation surgery in place of debulking surgery, although the risk of chemotherapy-induced gonadotoxicity should always be kept in mind.¹³ There is limited information on the impact of these chemotherapy regimens on reproductive function when managing YSTs. In the 1980s, the PVB regimen demonstrated improved survival rates with sustained remission in patients with advanced YSTs.¹⁴ Later, the bleomycin, etoposide, cisplatin (BEP) combination appeared to be the most active regimen.¹⁵ The effect of the BEP combination regimen following fertility-sparing surgery for ovarian YSTs was very good, with a 94% 5-year survival rate and 90% disease-free survival rate.¹⁶ The reproductive outcomes of patients with malignant germ cell tumor in five major series are shown in Table 1.^{16–20} The rate of return to normal menstruation in all cases was 78% (88/113), and the overall successful pregnancy rate was 57% (30/53).^{16–19} In our case, the right ovarian YST was diagnosed and managed at 13 years of age, just 1 year after her menarche. Conservative and

Table 1
The reproductive outcomes of patients with malignant germ cell tumor in five major series.

Author/year	Histology (n)	Stage (n)	Surgery (n)	CT regimen (n)	Fertility evaluation (n)	Return of menstruation (n)	Attempted pregnancy (n)	Pregnancy/patient (n)	Remarks
Kang et al ¹⁷ /2008 (n = 20)	YST (18) Mixed (2)	I (10) II (4) III (6)	USO (15)	BEP (20)	20	15	6	2	Live-birth deliveries and no complications
de La Motte Rouge et al ¹⁶ /2008 (n = 52)	YST (30) Mixed (22)	I (34) II (1) III (14) IV (3)	USO (27) UO (10) UC (4)	BEP (52)	52	39	16	12	Normal pregnancy with normal children: 15 of 19 (79%) Ongoing pregnancy: 1 of 19 (5%) Miscarriage: 2 of 19 (11%) Termination: 1 of 19 (5%) Delivered without complication (all live-birth deliveries)
Ayhan et al ¹⁸ /2005 (n = 29)	YST (22) Mixed (7)	I (16) II (1) III (9) IV (3)	USO (8) UC (7)	BEP (29)	15	10	5	3	Delivered without complication (all live-birth deliveries)
Mitchell et al ¹⁹ /1999 (n = 69)	IT (11) YST (20) Mixed (32) Non-dys (6)	I (35) II (7) III (22) IV (5)	USO (45) UC (5)	BEP (31) PVB (11) CEB (7) BOP (3) Others (7)	26	24	26	11	—
Ezzat et al ²⁰ /1999 (n = 67)	Dys (33) IT (18) YST (10) Mixed (6)	I/II (44) III (14) IV (3) NA (6)	USO (53)	BEP (30) PVB (9) Other (28)	44	NA	—	16	—

Attempted pregnancy = attempt to get pregnant; BEP = bleomycin, etoposide, and cisplatin; BOP = bleomycin, vincristine, and cisplatin; CT = chemotherapy; CEB = carboplatin, etoposide, and bleomycin; dys = dysgerminoma; IT = immature teratoma; mixed = mixed germ cell tumor; n = number of patients; non-dys = nondysgerminoma; NA = no data available; PVB = cisplatin, vinblastine, and bleomycin; UC = unilateral cystectomy; UO = unilateral oophorectomy; USO = unilateral salpingo-oophorectomy; YST = yolk sac tumor.

comprehensive staging surgery followed by cisplatin-based chemotherapy successfully treated this patient. In addition, the return of her menstrual cycle after treatment suggested a minimal effect on ovarian function. Finally, the natural conception with successful term delivery of a healthy fetus further supported the results of previous studies, summarized in Table 1, that most patients with comprehensive staging but fertility-sparing surgery followed by cisplatin-based chemotherapy can have an excellent disease-free survival. Thus, it can be said that ovarian function and future reproductive outcome can be predicted.

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